UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/126,559	07/30/1998	DANIEL J. CAPON	11068-043-999	9053

7590 09/22/2004

Jones Day
222 East 41st Street
New York, NY 10017

EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/126,559	CAPON ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 May 2004*.

2a)☐ This action is **FINAL**. 2b)☑ This action is non-final.

3)☒ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *112-131* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *112-131* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6-3-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Currently, claims 112-131 are pending and under consideration in the application. In the prior action, mailed on July 15, 2003, claims 1, 4, 8, 55, and 57 were pending and rejected. In the Response, filed on May 17, 2004, the Applicant amended claims 112, 113, 115, and 116, and added new claims 117-131.

2. It is noted that the Applicant refers in the Response (page 17) to a copending application 08/875082 purportedly filed by the current inventors. However, the application by this number does not appear to be commonly owned or assigned, to have the same inventors, or to describe related subject matter. It is thus not clear what application Applicant is referring to.

3. This action is being made Non-Final due to the presence of new rejections, raising new issues, and not necessitated by amendment.

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on June 3, 2004, is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

5. It is noted that several of the documents listed in the IDS have been crossed out. These documents are either not references that may be properly cited or considered as applicable against the claims (e.g. search reports citing other references, the pre-grant publication of the present application), or are references that have already been made of record in the present application.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. **(New Rejection- Necessitated by amendment)** Claims 112-131 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims read on methods of culturing "a sample of host cells" in the presence of an anti-viral drug, wherein the host cells have "introduced thereto a plurality of resistance test vectors." The claims are rejected for two reasons.

First, it is not clear what is meant by a "sample of host cells," in that it is not clear what the host cells are a sample of.

Second, it is not clear from the claim language if each host cell comprises a plurality of test vectors, or if the Applicant is claiming a method involving a plurality of host cells, comprising different host cells which have been transfected with different resistance test vectors as described by the claims.

Clarification is required.

For the purposes of this action, it is assumed that "a sample of host cells" merely describes a composition of multiple such cells, and that the claims are drawn to methods of culturing a set of host cells comprising different host cells which have been transfected with different resistance test vectors.

8. **(New Rejection)** Claims 112-114, and 117-121 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims read on methods wherein the methods involve additional steps of comparing the activity of indicator genes in "a corresponding sample of host cells" transfected with a "corresponding plurality of resistance test vectors." It is not clear what the term "corresponding to" relates to. It is suggested that part (c) of the claim be amended to read on a step of comparing the indicator gene activity in (b) to the activity in - - a sample of host cells corresponding to the host cells cultured in (a), wherein the cells are cultured in the absence of the HCV anti-viral drug- -.

9. **(New Rejection)** Claims 116, and 127-131 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 116 is treated as representative. This claim is rejected because it is not clear how the method of step determines the susceptibility of the virus as indicated in the description of part (b) of the claim. It is suggested that the term "susceptibility of the HCV" or "susceptibility" in parts (b) and (c) of the claim be replaced with the term "activity of the indicator gene," and that the last part of the claim be amended to

indicate that an increase in the activity of the indicator gene at the second time point relative to the first time point indicates anti-HCV drug-resistance of the HCV viral population (or other language clarifying the relationship between the activity of the indicator gene and viral susceptibility to the drug).

10. **(Prior Rejection-Withdrawn)** Claims 112-115 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of determining if a particular viral is susceptible to an anti-viral drug, does not reasonably provide enablement for methods of determining if a viral population is so susceptible. In view of the amendments to the claims, and the arguments pursuant thereto, the rejection is withdrawn.

11. **(Prior Rejection-Withdrawn)** Claims 112-116 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of determining HCV susceptibility to an anti-viral drug that inhibits or prevents viral replication, does not reasonably provide enablement for any anti-viral drug. In view of the Applicants arguments in traverse, the rejection is withdrawn.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. **(Prior Rejection- Maintained)** Claims 112-114, and 116 were rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over U.S. Patent Number 6,127,116, issued to Rice et al. These describe methods of determining the susceptibility of a hepatitis C virus population to an anti-HCV drug. The Applicant traverses the rejection of the claims over the teachings of Rice by asserting that Rice provides no motivation for the modification of the disclosed methods for determining susceptibility of HCV isolates for particular drugs such that the methods involve the testing of multiple test vectors for the effect of anti-HCV drugs on the various isolates of HCV that make up a HCV population in a patient. The Applicant bases this assertion on the supposed failed of Rice to teach that there is variation in the HCV population within a single patient.

This argument is not found persuasive because Rice does indeed teach that variants of HCV may arise in HCV infected patients. Even if it were assumed that the paragraphs cited by the Examiner in the prior rejection do not demonstrate that Rice was aware that multiple isolates may be present in a single patient, the teachings of Rice overall still suggest the determination of the effect of anti-HCV drugs on multiple isolates of HCV from a patient. Such motivation can be found in the additional teachings in (e.g.) column 7, lines 10-50, and column 38, lines 9-28 of the patent. These paragraphs teach both that variants and anti-HCV drug resistant variants of the virus may arise in infected individuals, and suggests that the fact is important for the design and evaluation of anti-HCV therapies.

In particular, the teachings in column 38 provide both suggestion and motivation for modifying the disclosed methods such that multiple test vectors are used to determine susceptibility. In lines 15-17 of the column, the patent states that "variability manifests itself in

the infected patient over time and in the considerable diversity observed between different isolates." The patent therefore indicates that multiple isolates and variants may be found within a single patient. In lines 25-28, the patent further states "Resistant mutants can then be used... to evaluate new therapeutic formulations, or in screening assays for effective anti-HCV drugs." Lines 17-19 also state that the generation of such variants within an individual is "likely to be an important consideration in the design and evaluation of HCV mono and combination therapies." Thus, the patent suggests the creation of test vectors from these variants to determine their susceptibility to anti-HCV drugs. Because the reference both provides this suggestion, and indicated that there may be multiple such variants in a patient, it would have been obvious to those in the art to use multiple test vectors, each representing a different variant, in such susceptibility assays. In view of these additional teachings, the Applicant's assertion that the reference fails to suggest or provide motivation for using methods such as those claimed are not found persuasive. The rejection is therefore maintained for the reasons above, and the reasons of record.

14. **(Prior Rejection- Maintained)** Claim 115 was rejected under 35 U.S.C. 103(a) as being unpatentable over Rice as applied to claims 112-114, and 116 above, and further in view of the teachings of Fridland et al., U.S. patent 5,576,177, and Bornstein et al., Reissue 29,955. The Applicant traverses this rejection on the same grounds as argued with respect to the rejection of claims 112-114 and 116 over Rice. No additional arguments have been presented. The rejection is therefore maintained for the reasons above, and the reasons of record.

15. **(New Rejection- Necessitated by Amendment)** Claims 117-121, and 127-131 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rice as applied to claims 112-114, and 116 above. The teachings of Rice have been described in part above. The indicated claims limit the claimed methods to embodiments targeting specific HCV proteins, or to embodiments of the claimed invention wherein the indicator gene is luciferase.

In addition to the teachings described above and in the prior actions, Rice also suggests potential targets for anti-HCV therapy, including the NS5b, and the NS3 and NS4a proteins. Column 25, lines37-45, and column 26 lines 31-65. Further, the reference also teaches a method for detecting the activity of NS3 in a cell through use of vectors encoding the NS3 and NS4a proteins. Column 15, lines 3-35. Because the patent teaches that this model is effective for the detection of NS3 activity, and also suggests the use of the models disclosed in the application for the identification of anti-HCV drugs that target the NS3 protein, it would have been obvious to those in the art to use such a model comprising genes encoding both the NS3 and NS4a proteins in methods for the identification of the anti-NS3 drugs. Thus, the reference provides teachings and suggestions that would have lead those in the art to methods involving the transformation of cells with genes encoding one or more of the indicated HCV proteins for the identification of anti-HCV therapeutics.

As described in the Office action mailed in November 2002, the Rice reference also teaches the inclusion of indicator genes in the HCV clones used in the disclosed methods. Column 36, lines 27-39. Further, luciferase is among the markers suggested by the patent for use in the claimed methods. Id. Thus, the reference renders obvious embodiments wherein the indicator gene is a luciferase gene.

The reference therefore renders the claims obvious.

16. **(New Rejection- Necessitated by Amendment)** Claims 122-126 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rice as applied to claims 112-114, and 116-121, and 127-131 above, and further in view of Fridland and Bornstein as applied to claim 115 above. The indicated claims limit the method of claim 115 (described in the prior action) to embodiments targeting specific HCV proteins, or to embodiments of the claimed invention wherein the indicator gene is luciferase. For the reasons indicated above with respect to claims 115, and claims 117-121, and 127-131, the cited references render the claimed methods obvious.

Double Patenting

17. **(Prior Rejection- Restated as Necessitated by Amendment and Maintained)** Claims 112-116 were rejected in the prior action under the judicially created doctrine of obviousness-type double patenting as being unpatentable over either claims 1, 4, 7-11, 13,14,46-49,51-53,70-73, and 78-83 of U.S. Patent 5,837,464 in view of Lu et al. and Wang et al., or claims 1,2,18,24-27, and 30-42 of U.S. Patent No. 6,242,187, in view of Lu et al. or Wang et al. The rejections are hereby restated such that the claims are rejected over the teachings of the indicated commonly owned or assigned patents in view of Lu or Wang, and further in view of Rice. Further, the rejection is extended to new claims 117-131 (for the reasons indicated above with reference to the Rice patent). The Applicant traverses the rejection on the grounds that neither Lu nor Wang teach or suggest the adaptation of the claimed methods for determining susceptibility of HIV or

HBV to antiviral drugs could be adapted t o determining susceptibility of HCV for such drugs. This argument is not found persuasive.

It is first noted that, while the claims of the two patent refer to anti-HIV or anti-HBV drugs, neither of the patents limits the scope of patient derived segments that are being assayed for drug susceptibility. Rather, the claims are merely identifying a set of drugs, susceptibility to which is being determined. Further, the patents each indicate that the claimed methods are "related to drug susceptibility and resistance tests useful in providing an optimal therapeutic regimen for the treatment of **various viral diseases**, including for example, HIV/AIDS and hepatitis." Column 1 in each of the patents. Thus, the references clearly indicate that the claimed methods are useful for providing susceptibility information about any viral infection.

Because the claims of the patents are not limited to methods of determining the susceptibility of particular viruses to anti-viral drugs, it would have been obvious to those in the art that the methods could be applied to determine the susceptibility of any virus to the indicated drugs. Lu and Wang each demonstrate that those in the art would have looked to the teachings of these patents to identify therapeutics against HCV. From these combined teachings, it would therefore have been obvious to apply the claimed methods to the identification of therapeutics effective against HCV. Because the methods of the patents are not limited as to what viruses the anti-viral drug susceptibility is being determined in, the teachings as described above and in the prior actions demonstrate the presently claims methods are obvious variations of the methods claimed in the patents.

While the present claims are directed to the identification of susceptibility of HCV to anti-HCV drugs, there is no limitation provided in the application as to what constitutes an anti-

HCV drug. Rather, the claims themselves are directed to methods of determining if the indicated drugs have efficacy against the virus. Thus, it would have been obvious to those in the art to use the claimed methods to determine if drugs effective against either of HIV or HBV would also be effective against HCV.

It is noted that the claims have been amended to require that the methods involve the culturing of a sample of host cells comprising a plurality of resistance test vectors, and wherein the methods are testing for the activity , rather than the expression of the indicator genes. However, these amendments are also deemed obvious variations from the methods claimed in the patents. This is due to the teachings of Rice as described above in response to the traversal of the rejection over this reference. From these teachings, as indicated above, it would have been obvious to modify the claims of the commonly owned patents such that multiple resistance test vectors are used. The claims of the patents are generic to the presently claimed inventions. While the claims are of patents do not require multiple vectors, they also do not exclude them.

For these reasons, and the reasons of record, the rejection is maintained.

18. **(Prior Rejection- Restated and Maintained)** Claims 112-114 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 5, and 6 of copending Application No. 10/139,069. The rejection is hereby restated such that the claims are rejected over claims 8, 9, 12, and 13 of the copending application further in view of Rice as applied above. The rejection is also extended to claims 115, and new claims 117-126.

It is first noted that the claims of the copending application previously cited are directed to methods involving the testing of different sets of test vectors each cultured in the presence of a test compound, rather than the same set of test vectors cultured in the presence and the absence of a test compound. However, claims 8, 9, 12, and 13 of the co-pending application are directed to the later methods.

The applicant traverses the rejection on the grounds that the claims of the copending application are directed to methods of determining a change in susceptibility of an HCV test sequence relative to a reference HCV sequence whereas the current claims are directed to methods of determining susceptibility of a HCV population to an anti-HCV drug. The Applicant further asserts that there is no claim or suggestion in the application suggesting the currently claimed inventions drawn to methods of determining the susceptibility of a viral population as opposed to a test HCV.

With respect to the first ground of traversal, it is noted that the claims of the copending application do not limit the claims to methods of determining if a single HCV is susceptible to an anti-HCV drug. While the claims are drawn to method of determining if a test HCV has such susceptibility, the claims do not exclude embodiments wherein multiple HCV test vectors are tested at the same time. This is because the claims are drawn to methods *comprising* the testing of a single test vector. The term "comprising" is an open term, allowing for the inclusion of additional steps. Because the current claims are drawn to methods of testing the susceptibility of plurality of test vectors, it inherently falls within the category of methods comprising the testing of a single vector.

The Applicant's second argument in traversal is that the copending application does not suggest the testing of a plurality of vectors, as is described by the amended claims. It is noted that the rejection has been restated in view of the amendment such that the claims are rejected over the copending application in view of the Rice reference as described above. From these combined teachings, it would have been obvious to those in the art to modify the claimed methods of the copending application such that they are determining the susceptibility of a viral population using a plurality of host cells comprising different cells having introduced thereto a plurality of different test vectors. The rejection, as restated, is therefore maintained.

Conclusion

19. No Claims are allowed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

JAMES HOUSEL 9/20/04
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600